

IN THE CLAIMS

Please amend claims, as shown below. Please cancel claim 17 without prejudice.
Please add new claim 26. The following listing of claims replaces all prior listings.

1-11 (Canceled).

12. (Currently amended) A method for screening for molecules having an affinity for an active protein in a complex mixture of proteins from a biological source, employing a combinatorial chemical library, the combinatorial chemical library comprising a mixture, the mixture including a plurality of members of the formula

$R^* (F - L) - X$

wherein:

X is a ligand selected from a group consisting of biotin, deiminobiotin, dethiobiotin, 1,2-dihydroxyethane, 1,2-dihydroxycyclohexane, digoxigenin, maltose, oligohistidine, glutathione, 2,4-dinitrobenzene, phenylarsenate, ssDNA, dsDNA, a peptide, or a polypeptide, a metal chelate, a saccharide, rhodamine, and hapten;

L is a bond or alkylene or an alkyleneoxy chain linking group of from 1 to 6 alkyleneoxy groups, wherein said alkyleneoxy groups are of from 2 to 3 carbon atoms, which is the same in each of the members of said combinatorial chemical library;

F is a sulfonyl functional group reactive at an active site of a protein member, which functional group comprises the same reactive functionality in each of the members of said combinatorial chemical library, and

R is a group of less than 1kDa, that is different in each of the members of the combinatorial chemical library, wherein R is selected from a group consisting of alkyl, pyridyl, substituted pyridyl, imidazole, pyrrole, thiophene, furan, azole, oxazole,

aziridine, aryl, substituted aryl, amino acid, peptidyl, quinoline, oligonucleotide and carbohydrate group;

the * intends that R is a part of F or L; and

wherein members of said combinatorial chemical library have different on rates with said protein member, and wherein members of said combinatorial chemical library react with an active site of said protein member, said method comprising:

(1) combining said combinatorial chemical library with said complex mixture of proteins, in an active form and an inactivated form, said combinatorial chemical library under conditions for reaction of said sulfonyl functional group with active proteins to form a conjugate;

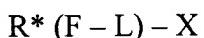
(2) isolating conjugates from said active and inactivated complex mixture of proteins; and

(3) comparing conjugates formed with said active and inactivated complex mixtures of proteins;

whereby conjugates in said active complex mixture absent in said inactivated complex mixture are comprised only of active proteins reactive with members of said chemical combinatorial library.

13. (Canceled).

14. (Currently amended) A method for screening for molecules having an affinity for an active target protein in a complex mixture of proteins from a biological source, employing a combinatorial chemical library of activity based probes, the combinatorial chemical library comprising a mixture, the mixture including a plurality of members of the formula



wherein:

X is a ligand selected from a group consisting of biotin, deiminobiotin, dethiobiotin, a vicinal diol, ~~1,2 dihydroxyethane~~, ~~1,2 dihydroxycyclohexane~~, digoxigenin, maltose, oligohistidine, glutathione, 2,4-dinitrobenzene, phenylarsenate, ssDNA, dsDNA, a peptide, ~~or~~ of a polypeptide, a metal chelate, a saccharide, rhodamine, fluorescein, and hapten;

L is a bond or alkylene or an alkyleneoxy chain linking group of from 1 to 6 alkyleneoxy groups, wherein said alkyleneoxy groups are of from 2 to 3 carbon atoms, which is the same in each of the members of said combinatorial chemical library;

F is a sulfonyl functional group that is the same in each member of said combinatorial chemical library; and

R is a group of less than 1kDal, that is different in each of the members of the combinatorial chemical library, wherein R is selected from a group consisting of alkyl, pyridyl, substituted pyridyl, imidazole, pyrrole, thiophene, furan, azole, oxazole, aziridine, aryl, substituted aryl, amino acid, peptidyl, quinoline, oligonucleotide and carbohydrate group;

the * denotes that R is a part of F or L;

wherein members of said combinatorial chemical library react with an active site of said protein member,

said method comprising:

(1) combining a first portion of said complex mixture of proteins with said combinatorial chemical library under conditions for reaction of said sulfonyl group with active proteins in said complex mixture of proteins to form conjugates;

(2) combining a second portion of said complex mixture of proteins, that has been inactivated, with said combinatorial library under the same reaction conditions as in

(1)

(3) isolating conjugates from said first and second portions of said complex mixture of proteins; and

(4) comparing conjugates formed from said first portion of said complex mixture of proteins with conjugates formed from said second portion of said complex mixture of proteins to determine the degree of activity of the total target protein as compared to active target protein.

15. (Canceled).

16. (Previously presented) A method according to claim 14, wherein said members of said combinatorial chemical library of activity based probes have differing on-rates with respect to said active proteins.

17. (Canceled).

18. (Previously presented) A method according to claim 14, wherein X is biotin.

19-20. (Canceled).

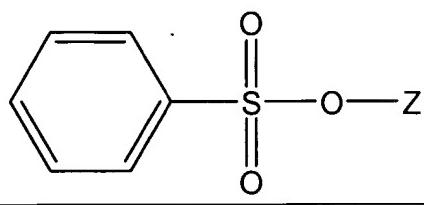
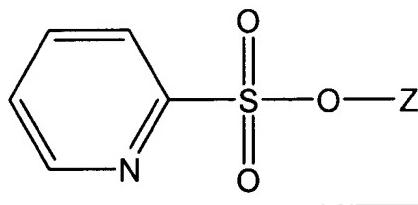
21. (Previously presented) A method according to claim 14, wherein F is sulfonate, sulfate, sulfinate, or sulfamate.

22. (Previously presented) A method according to claim 21, wherein F is sulfonate.

23. (Previously presented) A method according to claim 14, wherein said second portion of said complex mixture of proteins has been inactivated by heating.

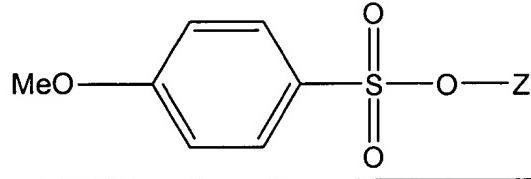
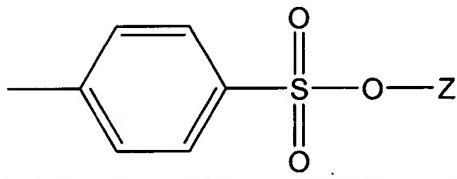
24. (Currently amended) A method according to claim 14, wherein said combinatorial chemical library of activity based probes comprises at least two of

sulfonate 1 - sulfonate 11 and sulfonate 15 - sulfonate 17, having the following structures:



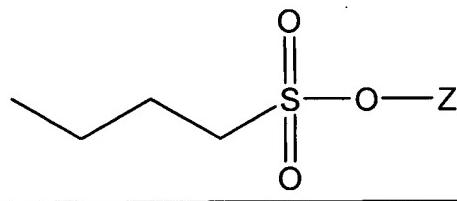
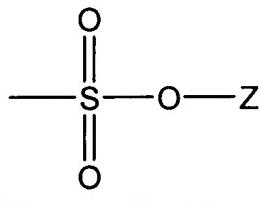
Sulfonate 1

Sulfonate 2



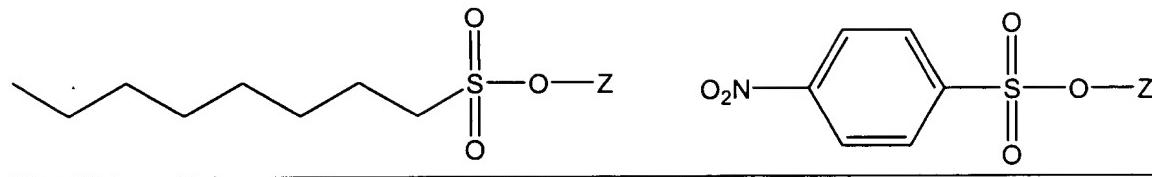
Sulfonate 3

Sulfonate 4

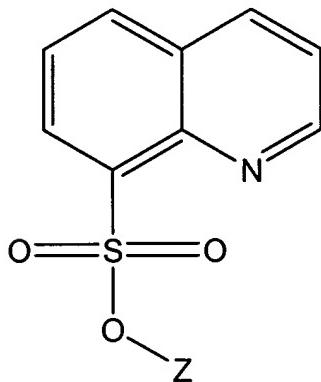


Sulfonate 5

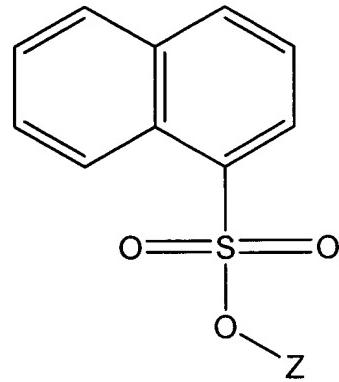
Sulfonate 6



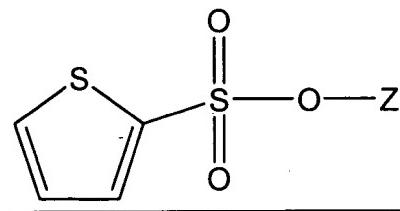
Sulfonate 7



Sulfonate 8



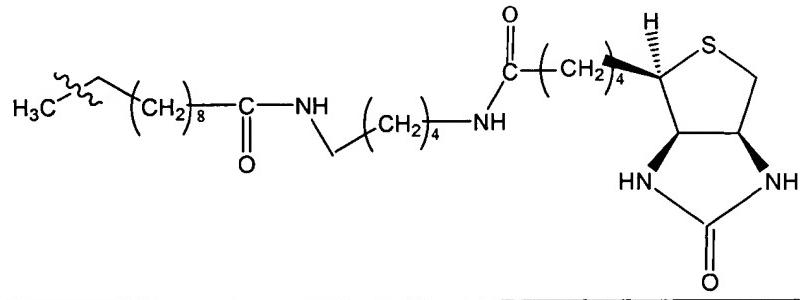
Sulfonate 9



Sulfonate 10

Sulfonate 11

wherein in Sulfonate 1-Sulfonate 11, Z is a moiety having the structure:



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25. (Canceled).

26. (New) A method according to claim 14, wherein the vicinal diol is 1,2-dihydroxyethane or 1,2-dihydroxycyclohexane.